Subcommittee on Criminal Justice, Drug Policy and Human Resources

Opening Statement of Chairman Mark Souder

"RU-486: Demonstrating a Low Standard for Women's Health?"

May 17, 2006

We are here today because there is a drug on the market associated with the deaths of at least eight women, nine life-life threatening incidents, 232 hospitalizations, 116 blood transfusions, and 88 cases of infection.[1] There have been more than 950 adverse event cases associated with RU-486, out of only 575,000 prescriptions[2] *at most*. Adverse events are typically underreported, since they are offered voluntarily by consumers and health care professionals, so it is most likely there are many more cases that we don't even know about.

It's very clear that there is a serious problem with RU-486, and failing to address this problem by disguising it, ignoring it, minimizing it or causing confusion is a shameful failure for anyone with the ability and desire to protect women from needless harm.

RU-486 is the common name for Mifeprex. It is produced by Danco Laboratories, a corporate entity located in the Cayman Islands which produces only that single drug, and nothing else. Mifeprex is approved by the FDA for the termination of pregnancy through 49 days of development. It is used in combination with another drug called misoprostol, which causes uterine contractions that expel the dead fetus. This is an off-label use for misoprostol, which contains a black-box warning against using the drug during pregnancy.

At least five of the deaths following the use of RU-486 have been the result of a toxic shock-like syndrome initiated by the bacteria Clostridium Soredellii. This bacteria is thought to exist in low numbers in the reproductive tracts of many women, and is normally combated by the immune system. Experts in immunology,[3] pharmacology,[4] and maternal-fetal medicine[5] have

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[1] Letter from David W. Boyer, Assistant Commissioner for Legislation, to Hon. Mark E. Souder, Chairman, Subcommittee on Criminal Justice, Drug Policy, and Human Resources, (May 2, 2006) (on file with Subcommittee).
[2] *Id*.
[3] *See,* Jeanette I. Webster and Esther M. Sternberg, *Role of the Hypothalamic-Pituitary-Adrenal Axis, Glucocorticoids and Glucocorticoid Receptors in Toxic Sequelae of Exposure to Bacterial and Viral Products*, Journal of Endocrinology 2004, 181:207-221 ("Natural and synthetic glucocorticoids protect against the lethal effects of many bacterial and viral components...agents that block the hypothalamic-pituitary-adrenal axis, as in…mifepristone…enhance lipopolysaccharide (LPS) and endotoxin lethality and LPS-induced fever. Even the normally endotoxin-nonresponsive C3H/HeJ mice could be made endotoxin sensitive by RU-486.")
[4] *See,* Ralph P. Miech, *Pathophysiology of Mifepristone-Induced Septic Shock Due to Clostridium Sordellii*, The Annals of Pharmacotherapy, September 2005, 39:

> "Mifepristone is a potent progesterone antagonist that, in addition to its ability to block glucocorticoid receptors, blocks progesterone receptors...Blockade of progesterone receptors…results in rejection of the developing placenta and death of the embryo. Prolonged ischemia of the decidua and the embryonic placenta causes necrosis [death] of these tissues.

suggested that because RU-486 interferes with the innate immune response, the bacteria, if present, is allowed to flourish, causing a widespread, multi-organ infection in the woman.

These infections are not accompanied by a fever, and the symptoms match those that are expected after taking the RU-486 regimen, including cramping, pain, bleeding, nausea, vomiting. Each of the women infected with C. Sordellii after taking RU-486 were dead within five to seven days.

To investigate the nature of this bacteria, the CDC and FDA held a scientific workshop last week called "Emerging Clostridial Disease." The workshop panelists noted that the rapid growth of the C. Sordellii bacteria in the RU-486 context likely forecloses effective treatment, and that there is no currently identifiable "window of opportunity" for treatment once a woman is infected, even with major interventions such as hysterectomy. The fatality rate has been 100% for the women who contracted C. Sordellii infection after RU-486.

Any other drug associated with a 100% fatal septic infection that kills otherwise healthy adults within days, with no apparent window for treatment, and associated with an exponential amount of severe reactions, would normally prompt an immediate withdrawal.

But we are talking about a drug regimen that is administered to cause an abortion, manufactured by a drug company based in the Caymen Islands, with no other drugs on the market, and therefore no incentive to voluntarily withdraw its product, no matter how dangerous. Many abortion advocates feel they have to defend this RU-486 because it is an alternative to surgical abortion. However, with eight deaths that we know about, RU-486 is ten to fourteen times more likely to be fatal than surgical abortion during the first seven weeks of pregnancy, the period during which the drug is administered.[6]

To continue defend this dangerous drug in light of mounting scientific evidence, injury and death is to allow one's zeal for abortion to truly distort their view about what's right for women's health. The ten-times-more-deadly danger posed by RU-486 should not be considered an "acceptable risk" that justifies keeping this drug on the market.

> Mifepristone also [causes] cervical dilation and liquefaction of the cervical mucus plug. The combined loss of a closed cervix and the protective cervical mucus plug permits contamination of the decidua and the intrauterine necrotic cells with aerobic and anaerobic bacteria from the normal vaginal flora."

[5] *See,* Sharon Worchester, *Mifepristone Deaths Raise Unanswered Questions*, Ob. Gyn. News, (October 1, 2005) at 13. (Quoting Dr. James A. McGregor)("Mifepristone has multiple pharmacologic properties that may interfere with innate immune responses to infection, toxin exposures, and inflammatory stimuli.")

[6] The mortality rate for women who procure a surgical abortion is 0.1 in 100,000 during the first eight weeks of pregnancy, the period for which RU-486 is available for women. Dr. Michael Green of Harvard based on usage rates of 460,000 and 4 deaths, suggested that the risk of death from chemical abortion is ten times greater. *See,* Michael F. Green, M.D., *Fatal Infections Associated with Mifepristone-Induced Abortion*, Dec. 1, 2005, N. ENGL. J. MED 353;22 *at* 2318. Current numbers suggest, however, eight deaths in the United States, while, according to the manufacturer, 575,000 women have used the drug. This works out to 1 in about 71,875, or 1.39 for every 100,000.

The approval of RU-486 was made under extreme political pressure from the Clinton Administration, which is well-documented in a recent report by Judicial Watch entitled "The Clinton RU-486 Files."[7] I ask that this report be included in the hearing record.

RU-486 was forced through the FDA using an extraordinary provision called "Subpart H," reserved only for drugs that treat life threatening illnesses, and for which existing treatments are insufficient.[8] It was obvious even to the drug sponsor that RU-486 did not fall within the narrow scope of Subpart H, saying that FDA's imposition of Subpart H was "unlawful, unnecessary, and undesirable."[9] But that did not deter the FDA in its extraordinary political complicity with President Clinton's Administration from forcing an abortion pill onto the market, no matter how distorted the approval process was, or what the price.

We are paying that price right now. Almost one thousand women have suffered adverse events after taking RU-486. We know that eight that have died. We have a responsibility to consider the dangers that this drug poses, and question whether FDA has the authority to remove it from the market in light of the severe problems associated with this drug and the manufacturer's failure to comply with post-marketing restrictions.

I anticipate that defenders of RU-486 will try to detract from the cold, hard facts, or cause confusion, by talking about other septic infections in other pregnancy situations. This tactic ignores what panelists reported at last week's CDC conference: that *Mifeprex compromises the innate immune system, providing an environment for rapid growth of the deadly infection*.

C. Sordellii infection in the RU-486 context is 100% fatal, with no opportunity for intervention. To ignore the immune system connection with Mifeprex, or to say that there have been "only five" such deaths, and advocate only for better surveillance and informed consent, will be no comfort to the family of the next woman who dies suddenly after taking RU-486.

To the shallow objection that those of us who are pro-life have no business looking into the problems associated with RU-486, let me respond: that is a smokescreen, and it is incredibly shameful. Anyone who honestly cares about women's health has got to take a critical look at the potential dangers of this drug. To argue otherwise, on the basis that this is simply an "abortion" issue, is to demonstrate a blind allegiance to abortion at any cost, including women's lives.

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[7] A Judicial Watch Special Report: The Clinton RU-486 Files, The Clinton Administration's Radical Drive to Force an Abortion Drug on America, April 26, 2006. Available at http://judicialwatch.org/archive/2006/jw-ru486-report.pdf (last visited May 17, 2006).

[8] 21 CFR 314.500 (1999).

[9] Letter to FDA/CDER, Office of Drug Evaluation III, Division of Reproductive and Urologic Products, from Sandra Arnold, Vice President, Corporate Affairs of the Population Council, (Sept. 6, 2000) [Cited in Citizen Petition re: Request for Stay and Repeal of the Approval of Mifeprex (mifepristone) for the Medical Termination of Intrauterine Pregnancy through 49 Days' Gestation, (Aug. 21, 2002), on file with the subcommittee].

Representing the FDA on the first panel is Dr. Janet Woodcock, Deputy Commissioner for Operations. On our second panel, we'll hear from Monty Patterson, the father of Holly Patterson, who was 18 years old when she died after taking RU-486; Dr. Susan Wood, Former FDA Asst. Commissioner for Women's Health; Dr. Lisa D. Rarick, of RAR Consulting; Dr. Donna Harrison, a Member of the Mifeprex Subcommittee of the American Association of Prolife Obstetricians and Gynecologists; and Carter Snead, Associate Professor of Law at the University of Notre Dame, and former General Counsel for the President's Council on Bioethics.

I wish to note that the Medical Director for Danco, the Cayman Islands-based manufacturer of RU-486, initially agreed to testify at this hearing, but pulled out two days ago. I intend to follow up with Danco to request answers in a sworn affidavit to critical questions regarding Danco's failure to comply with post-marketing restrictions for RU-486.

Last of all, I want to note that I notified the FDA last December that this Subcommittee would conduct a hearing into RU-486. [10] FDA's compliance with this oversight committee's document requests has been quite frustrating; we were getting critical documents related to our December request as late as last night. This hearing is not the end of our document requests, and I invite better cooperation from the agency moving forward. Now that we are here, and that we have most of the documents we requested five months ago, it's time to seek some answers about what can be done to protect women from this deadly drug.

[10] Letter from Hon. Mark E. Souder, Chairman, Subcommittee on Criminal Justice, Drug Policy, and Human Resources, to Hon. Andrew von Eschenbach, M.D. (Dec. 21, 2005), at http://reform.house.gov/CJDPHR/News/DocumentSingle.aspx?DocumentID=38547.